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09/846,058	04/30/2001	Jay K.. Bass	10004190-1	4485

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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/846,058	Applicant(s) BASS ET AL.	
	Examiner Jon D. Epperson	Art Unit 1639	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 01 March 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: Please see attached sheets.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Advisory Action

1. Applicants' augments submitted for reconsideration under 37 C.F.R. § 1.116 (e.g., see 4/15/2004 Response, pages 1-7) were found to be non-persuasive for the reasons set forth below.

Maintained Rejections and/or Objections

Claim Rejections - 35 USC § 112, first paragraph

2. Claims 28, 29, 31, 35 and 37-45 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

Applicant's claims are directed to a broad genus of methods for fabricating arrays with different chemical moieties. All the methods employ the use of a substrate. However, the specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form said substrate. Thus, the claims encompass the use of virtually an infinite number of substrates whether they can be transformed into a substrate that contains a higher height uniformity in one direction or not (e.g., see claim 28; see also specification, page 21, line 20, "The substrates may be fabricated from any of a variety of materials"). Claim 45, for

example, reads; "[a] method of fabricating an array of multiple features of different chemical moieties on a surface of a substrate, comprising: (a) comparing height uniformity in a first direction and a second direction across a planar surface of a substrate to identify a first direction having higher substrate height uniformity than a second direction, wherein said first and second direction are planar to the said substrate, (b) placing the different chemical moieties in a row on said planar surface of the substrate lengthwise along the direction having the higher height uniformity ... in order to fabricate and array of multiple features" Thus, directions B-F (referring to Applicants' figure 6, which is reproduced below with slight modifications) will possess higher height uniformity than direction A with direction F (i.e., the "drawn" direction) having the highest height uniformity. However, Applicants' claims are not limited to depositing different chemical moieties along the "F" direction. In fact, Applicants claims read on depositing different chemical moieties along directions B-E and even along a direction between A and B that only varies in angle from A by an infinitesimal amount (i.e., virtually parallel to A). Thus, the current claim language does not limit the number of substrates because every material possesses two directions that differ in height uniformity (at least to some extent). Thus, the methods encompass substrates that do not possess a first direction that has "substantially" higher height uniformity than a second direction.

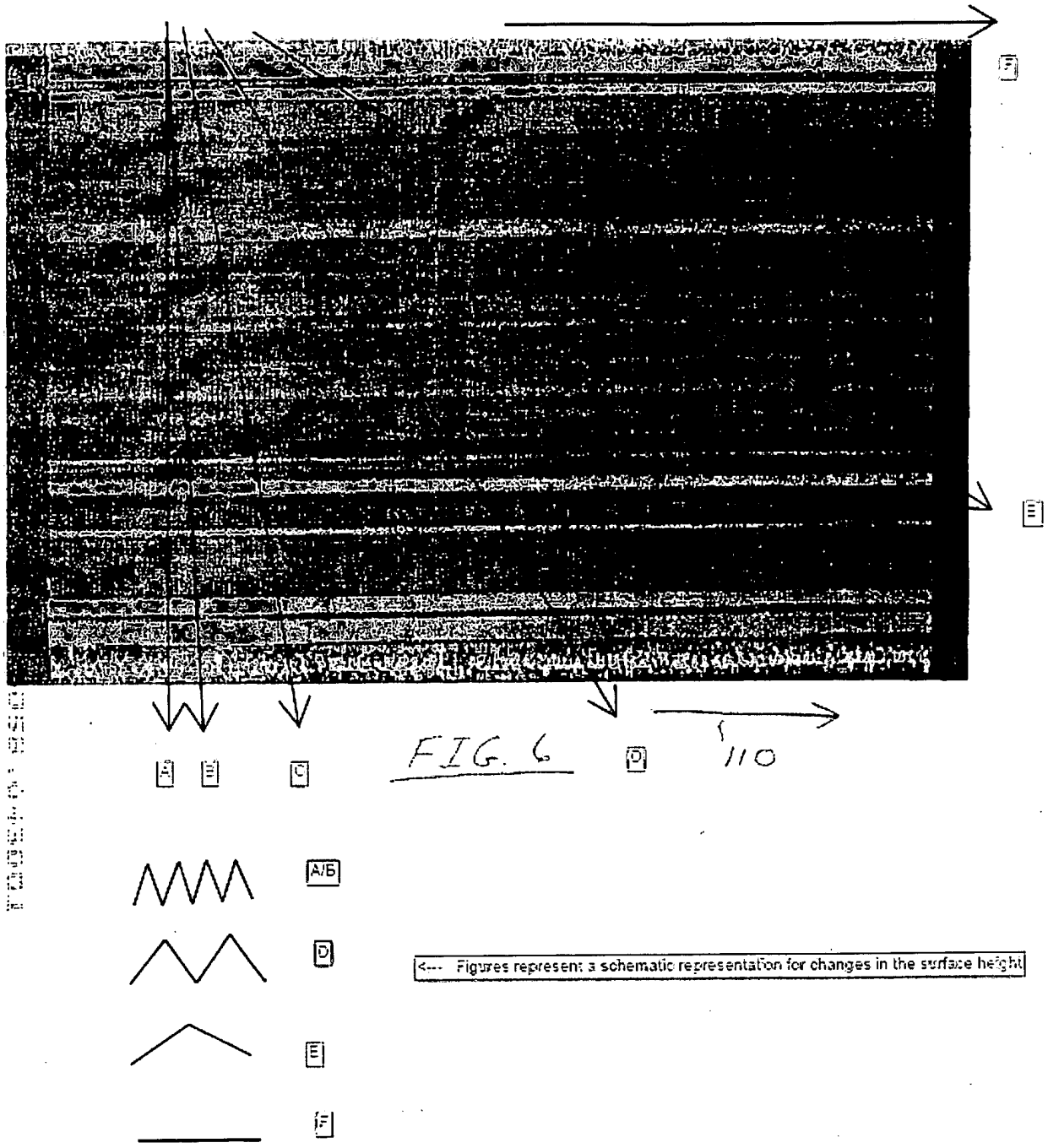

FIG. 6

This is especially true for substrates with "random" topology (e.g., see Smith, B. G. "Geometrical Shadowing of a Random Rough Surface" IEEE Transactions on Antennas and Propagation 1967, 5, 668-671; see also Bromberg, L. "Properties of

Aqueous Solutions and Gels of Poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide)-g-poly(acrylic acid)" *J. Phys. Chem. B* **1998**, *102*, 10736-10744 wherein pluronic gels are formed by random hydrophobic interactions). While a direction may be fortuitously found that bears higher height uniformity on a "random" substrate (at least to some infinitesimal degree, see above) such a substrate would not be amendable to the current process (even though it falls within the scope of the claims) because it would not lead to the deposition of materials in a direction with a "substantially" higher height uniformity (i.e., would not produce a useful result). Furthermore, Applicants' claims encompass many substrates that cannot be "drawn" into shapes that possesses "substantially" higher height uniformity because these materials are either too brittle or would react with other materials at the melting temperature required for fabrication (e.g., see Donald, I. W. "Production, properties and applications of microwire and related products" *J. Mater. Sci.* **1987**, *22*, 2661-2679, see especially, page 2665, section 2.1.2.3). In addition, the claims encompass "spherical" substrates (e.g., see also specification, page 9, lines 29 and 30, "Similarly, substrate 10 may be of any shape"; see also specification, page 21, paragraph 1) that possess tangential planar surfaces that would not foster a comparison of height uniformity because there is only one point at which a plane touches a sphere (i.e., the tangential plane).

Finally, no structural limitations are placed on the "chemical moieties" that are used to form the array either. Thus, virtually an infinite number of chemical moieties are also being claimed wherein no structural features and/or common structural characteristics are set forth (e.g., see Lauf et al., page 1, paragraph 4, "The preparation of

new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored.").

In contrast, Applicant's specification sets forth only one working example of a substrate with higher height uniformity in one direction than in another (e.g., see specification, page 3, paragraph 2; see also figures 6 and 7 wherein a planar glass substrate that was drawn in the molten state through a thin slot is set forth). Although the Applicants mention several other species that might be possible (e.g., see specification, page 21, paragraph 2 wherein both flexible and non-flexible materials are set forth including nylon, nitrocellulose, polypropylene, etc.), there is no evidence that any of these substrates were ever made and/or tested. Furthermore, there is no evidence presented that would suggest that any or all of the materials would likewise be amendable to a rolling process (like the one set forth for the drawn glass) that would impart a higher height uniformity. In addition, Applicants do not set forth any working examples of a chemical moiety. Although the specification sets forth several potential species (e.g., biopolymers such as carbohydrates, see specification, page 6, last paragraph) and cite several references such as Ser. No. 09/302898 for "Polynucleotide Array Fabrication", there is no evidence that any of these chemical moieties were ever used in accordance with the claimed method. Thus, Applicants have not even set forth a single working

example of the claimed method when the chemical entities are taken into account (i.e., no quid pro quo here).

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the claimed invention (e.g., see *In re Edwards*, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978); see also see also *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (CAFC 1991)). The "written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams formulas, etc., that fully set forth the claimed invention" (e.g., see *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966). In the present case, Applicants have not set forth even a single working example of the present invention. In addition, when there is *substantial variation within the genus*, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05). Here, the variation within the genus would be enormous because the nature of the claimed methods would depend on the nature of the substrates employed, which are virtually limitless. Furthermore, the vast numbers of substrates do not share any common attributes that would allow a person of skill in the art to extrapolate Applicants' limited species to the vast number of currently claimed substrates. Thus, the general knowledge and level of skill in the art do not supplement the omitted description because no known structure/function relationship and/or chemical properties exists that could otherwise be used to show possession of the enormous genus. In addition, there is no known generally accepted method for producing this wide array of substrates. Thus, the claims fail to satisfy the constitutional requisite of promoting the

progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result (e.g., all substrates), far beyond those means actually discovered or contemplated by the inventor (e.g., molten glass drawn into a flat rectangular shape), so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217; *Siegel v. Watson*, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119.

Response

3. Applicant's arguments directed to the above written description rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' arguments.

[1] Applicants argue that all of the elements are well known in the art and, as a result, they do not need to describe them in the specification and cite MPEP § 2163.02 in support of this position (e.g., see 3/1/07 Response, pages 6 and 7).

[1] Applicants' arguments do not rise to the level of factual evidence. See MPEP § 716.01(c): The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Here, Applicants cite no references to support this conclusion. Furthermore, Applicants cite no references to refute the Examiner's references of record.

[2] Applicants argue that the claim language function to exclude all "non inoperative" embodiments set forth by the Examiner (e.g., see 3/1/07 Response, page 7) including any of the non-inoperative substrates (e.g., see pages 7 and 8, section A, especially page 8, middle paragraph, "all other substrates which do not meet these claim limitations [e.g., higher height uniformity, drawn substrates] are outside the scope of the claims").

[2] The Examiner respectfully disagrees. Claim 45, for example, reads, "A method of fabricating an array of multiple features of different chemical moieties on a surface of a substrate, comprising: (a) comparing height uniformity in a first direction and a second direction across a planar surface of a substrate to identify a first direction having higher substrate height uniformity than a second direction, wherein said first and second direction are planar to the said substrate, (b) placing the different chemical moieties in a row on said planar surface of the substrate lengthwise along the direction having the higher height uniformity ... in order to fabricate and array of multiple features" Thus, directions B-F (referring to Applicants' figure 6, which is reproduced below with slight modifications) will possess higher height uniformity than direction A with direction F (i.e., the "drawn" direction) having the highest height uniformity. However, Applicants' claims are not limited to depositing different chemical moieties along the "F" direction. In fact, Applicants claims read on depositing different chemical moieties along directions B-E and even along a direction between A and B that only varies in angle from A by an infinitesimal amount (i.e., virtually parallel to A). Thus, the current claim language, contrary to Applicants' assertions, does not limit the number of substrates because every

material possesses two directions that differ in height uniformity (at least to some extent). Therefore, Applicants' arguments are not commensurate in scope with the claims (i.e., Applicants' claims do encompass virtually an infinite number of substrates, see also Applicants' admission on page 9, paragraph 2 of the 3/1/07 Response, "Simply because a planar substrate may have a 'random topology' does not necessarily mean that the surface does not have a 'first direction having higher substrate height uniformity than a second direction'"). Furthermore, it is clear that Applicants are not even in possession of an invention for depositing chemical moieties along lines B, C, D and E for "drawn" substrates because these directions would not "substantially" reduce the heterogeneity that might otherwise provide for a more favorably screening array i.e., making the comparison would not be useful (e.g., see Background of Invention).

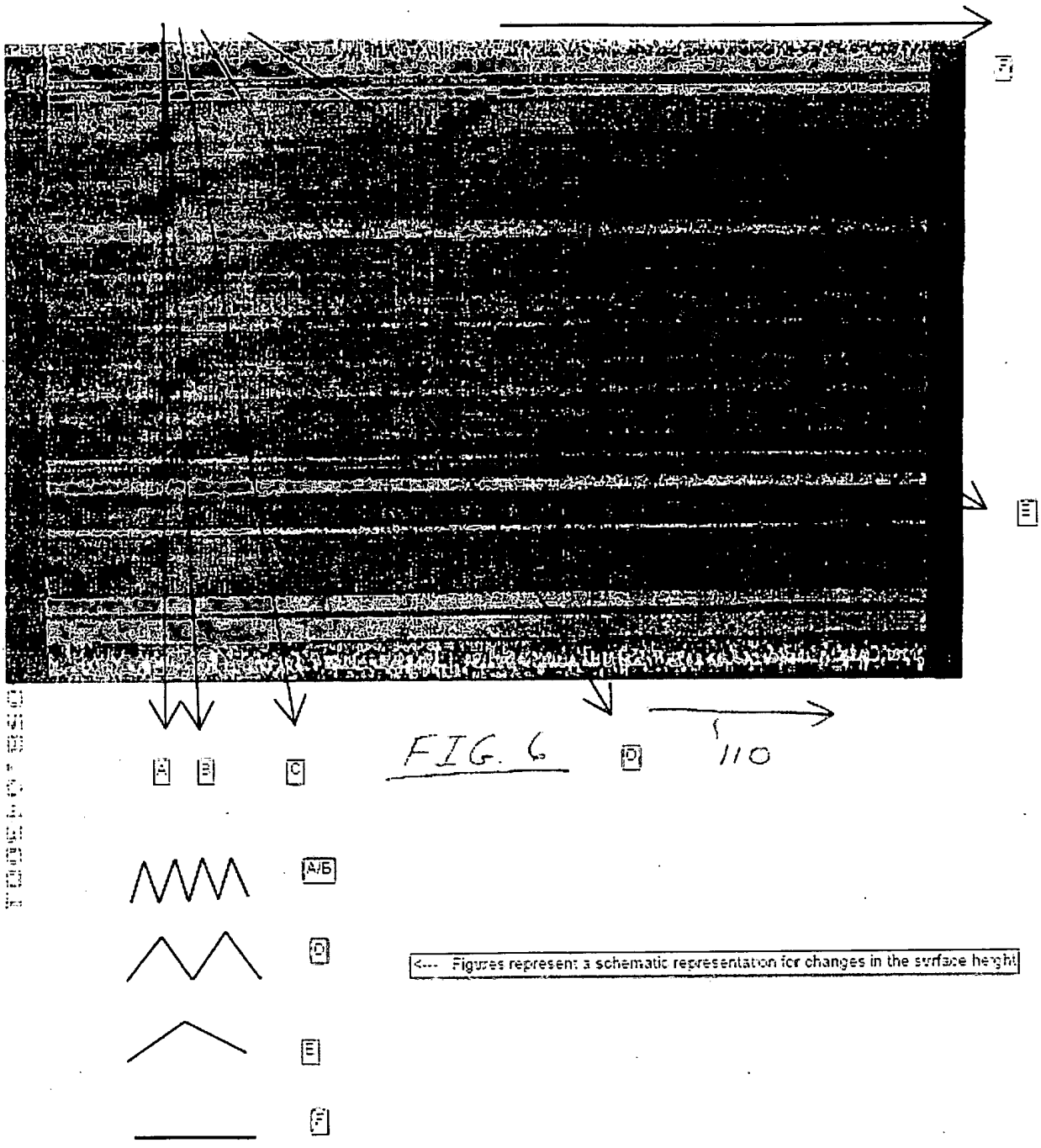

FIG. 6

[3] Applicants argue, "[s]imply because a planar substrate may have a 'random topology' does not necessarily mean that the surface dose not have a 'first direction

having higher substrate height uniformity than a second direction.' Rather, it means that in order to determine the height uniformity of the substrate surface in the different directions one might have to integrate the various variations along the chosen direction to come up with the overall surface variations along the chosen direction" (e.g., see 3/1/07 Response, pages 8 and 9, especially page 9, middle paragraph).

[3] Applicants do not mention or discuss techniques for "integration" in their specification. Such scope, if incorporated, would represent new matter. This fact only serves to highlight the Examiner's point that Applicants are not in possession of the full scope of the claimed invention.

[4] Applicants argue, "implicit within the claim language ... one of skill in the art [interpreting said language] would ... understand that Claims 37 and 38 inherently include a substrate that does in face have 'a higher height uniformity along a first direction than along a second direction ... [and] not doubt that Applicants had possession of the claimed invention." (e.g., see 3/1/07 Response, pages 9 and 10,).

[4] Whether the claimed substrate actually possesses a higher height uniformity is irrelevant because the increase may represent only an infinitesimal increment.

[5] Applicants argue, "the substrate contain a planar surface (i.e., claims 27 and 45) or that the substrate be drawn (i.e., Claim 29). Hence ... substrates that do not have a planar surface (e.g., spherical substrates) ... are excluded from the metes and bounds of the claims" (e.g., see 3/1/07 Response, pages 10 and 11).

[5] The Examiner respectfully disagrees. A spherical substrate possesses a tangential "planar" surface. Therefore, Applicants' arguments are not commensurate in scope with the claims.

[6] Applicants argue, "not all chemical moieties are being claimed, rather, only those that are capable of being deposited via the use of an inkjet printer. That being said, the ability to identify on a substrate surface [with] a higher substrate height uniformity does not depend on what type of chemical moiety is being used in the fabrication of the array" (e.g., see 3/1/07 Response, pages 11 and 12, especially paragraph bridging pages 11 and 12).

[6] While it may be true that the ability to identify a substrate surface with a higher height uniformity does not depend on what type of chemical moiety is being used in the fabrication of the array, that does not change the fact that According to Lauf et al. (see rejection above), "The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored." Thus, the vast majority of arrays produced by Applicants' methods may have no utility at all or, alternatively, be impossible to produce.

Accordingly, the written description rejection cited above is hereby maintained.

4. Claims 28, 29, 31, 35 and 37-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for forming an array of oligonucleotides on a rectangular substrate of drawn glass, does not reasonably provide enablement for methods that will lead to the production of "any" chemical moiety on "any" substrate surface. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". Some of these factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: Applicant's claims are directed to a broad genus of methods for fabricating arrays with different chemical moieties. All the methods employ the use of a substrate. However, the specification and claims do not place any limit on the number of atoms, the types of

atoms, or the manner in which said atoms might be connected to form said substrate. Thus, the claims encompass the use of virtually an infinite number of substrates whether they can be transformed into a substrate that contains a higher height uniformity in one direction or not (e.g., see claim 28; see also specification, page 21, line 20, "The substrates may be fabricated from any of a variety of materials"). Claim 45, for example, reads, "[a] method of fabricating an array of multiple features of different chemical moieties on a surface of a substrate, comprising: (a) comparing height uniformity in a first direction and a second direction across a planar surface of a substrate to identify a first direction having higher substrate height uniformity than a second direction, wherein said first and second direction are planar to the said substrate, (b) placing the different chemical moieties in a row on said planar surface of the substrate lengthwise along the direction having the higher height uniformity ... in order to fabricate and array of multiple features" Thus, directions B-F (referring to Applicants' figure 6, which is reproduced below with slight modifications) will possess higher height uniformity than direction A with direction F (i.e., the "drawn" direction) having the highest height uniformity. However, Applicants' claims are not limited to depositing different chemical moieties along the "F" direction. In fact, Applicants claims read on depositing different chemical moieties along directions B-E and even along a direction between A and B that only varies in angle from A by an infinitesimal amount (i.e., virtually parallel to A). Thus, the current claim language does not limit the number of substrates because every material possesses two directions that differ in height uniformity (at least to some extent). Thus, the methods encompass substrates that do not possess a first direction that has

"substantially" higher height uniformity than a second direction.

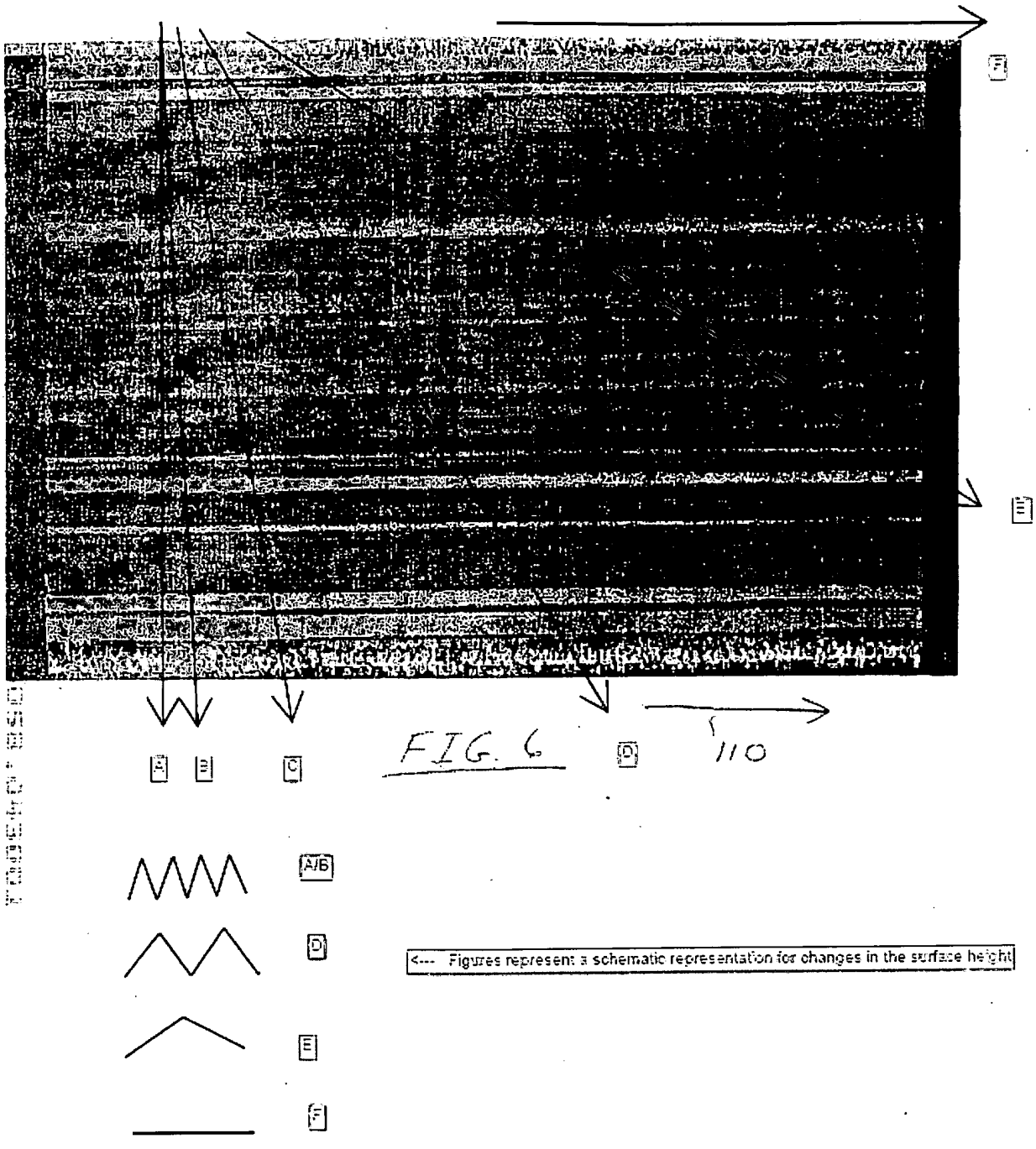

FIG. 6

This is especially true for substrates with "random" topology (e.g., see Smith, B. G. "Geometrical Shadowing of a Random Rough Surface" IEEE Transactions on

Antennas and Propagation 1967, 5, 668-671; see also Bromberg, L. "Properties of Aqueous Solutions and Gels of Poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide)-g-poly(acrylic acid)" *J. Phys. Chem. B* **1998**, *102*, 10736-10744 wherein pluronic gels are formed by random hydrophobic interactions). While a direction may be fortuitously found that bears higher height uniformity on a "random" substrate (at least to some infinitesimal degree, see above) such a substrate would not be amendable to the current process (even though it falls within the scope of the claims) because it would not lead to the deposition of materials in a direction with a "substantially" higher height uniformity (i.e., would not produce a useful result). Furthermore, Applicants' claims encompass many substrates that cannot be "drawn" into shapes that possesses "substantially" higher height uniformity because these materials are either too brittle or would react with other materials at the melting temperature required for fabrication (e.g., see Donald, I. W. "Production, properties and applications of microwire and related products" *J. Mater. Sci.* **1987**, *22*, 2661-2679, see especially, page 2665, section 2.1.2.3). In addition, the claims encompass "spherical" substrates (e.g., see also specification, page 9, lines 29 and 30, "Similarly, substrate 10 may be of any shape"; see also specification, page 21, paragraph 1) that possess tangential planar surfaces that would not foster a comparison of height uniformity because there is only one point at which a plane touches a sphere (i.e., the tangential plane).

Finally, no structural limitations are placed on the "chemical moieties" that are used to form the array either. Thus, virtually an infinite number of chemical moieties are also being claimed wherein no structural features and/or common structural

characteristics are set forth (e.g., see Lauf et al., page 1, paragraph 4, "The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored.").

(3 and 5) The state of the prior art and the level of predictability in the art: The level of predictability in the art is low or absent. For example, the methods encompass substrates that do not possess a first direction that has higher height uniformity than a second direction as required by independent claims 28, 37, 38 and 45. For example, the claims encompass the use of substrates with "random" topology (e.g., see Smith, B. G. "Geometrical Shadowing of a Random Rough Surface" IEEE Transactions on Antennas and Propagation 1967, 5, 668-671; see also Bromberg, L. "Properties of Aqueous Solutions and Gels of Poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide)-g-poly(acrylic acid)" *J. Phys. Chem. B* **1998**, *102*, 10736-10744 wherein pluronic gels are formed by random hydrophobic interactions) that would not be amendable to current process because the comparison would not produce a definitive result (i.e., a direction with higher height uniformity) and thus represent "inoperative" embodiments because the claimed comparison will not lead to a definitive result (i.e., one direction will not be better than the other). In addition, substrates that have been "drawn" using a thin slit, for example, which might reasonably be expected to produce a direction with higher

height uniformity does not encompass all substrates. For example, Applicants' claims encompass many substrates that cannot be "drawn" into shapes that possesses height uniformity because these materials are either too brittle or would react with other materials at the melting temperature required for fabrication (e.g., see Donald, I. W. "Production, properties and applications of microwire and related products" *J. Mater. Sci.* **1987**, *22*, 2661-2679, see especially, page 2665, section 2.1.2.3).

In addition, many of Applicants' claimed substrate shapes would likewise be inoperative. For example, claims encompassing spherical substrates (e.g., see also specification, page 9, lines 29 and 30, "Similarly, substrate 10 may be of any shape"; see also specification, page 21, paragraph 1) that possess tangential planar surfaces would not foster a comparison of height uniformity because any comparison of said directions would only provide information with regard to the same point on the substrate (i.e., the point at which the plane touches the sphere). Thus, no comparative result would be produced.

Finally, there are no known methods that enable the synthesis and/or characterization of the currently claimed chemical moieties (e.g., see Lauf et al., U.S. Patent Application No. 2004/0062911 A1; page 1, paragraph 4, "The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of

possible new compounds remains largely unexplored."; see also Newsam, J. M.; Schuth, F. "Combinatorial Approaches as a Component of High-throughput Experimentation (HTE) in Catalysis Research" Comb. Chem. Biotechnol. Bioeng. 1999, 61-1, 203-216, especially page 210, column 2, paragraphs 2-3 "Applications of HTE [High Throughput Experimentation] and combinatorial methods to heterogeneous catalysts are substantially different from those used in homogeneous catalysis ... First, we have little basis yet for formal library design, atomic-level active-site structure usually being, at best, poorly characterized. Second, detailed catalysts characterization is difficult. The averaged picture provided by X-ray and neutron scattering or EXAFS usually masks the active-site signatures, and local probes are likely to miss these critical, yet dilute fine details. Third, the optimal performance of a catalysts is a balance between reactor configuration, reaction conditions, and the details of the catalyst itself; a change in one of the three elements requires concomitant adjustment in the two others. Fourth, scale-up of catalyst preparation even from the laboratory scale can be difficult. Firth, many catalysts only attain theri desirable properties after time on stream, catalyst formation and deactivation processes being important in determining performance. Finally, the reaction conditions required for practical testing typically entail elevated temperatures and pressures, and various gas or liquid streams that might be flammable or toxic. Unsurprisingly, therefore, the field of accelerated combinatorial heterogeneous catalysis is still at an early stage of development" as another example of a catalyst library that falls within the scope of Applicants' claimed chemical moieties).

(4) The level of one of ordinary skill: The level of skill required would be high, most

likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have not even provided a single working example of the claimed invention. Although Applicants' specification sets forth only one working example of a substrate with higher height uniformity in one direction than in another (e.g., see specification, page 3, paragraph 2; see also figures 6 and 7 wherein a planar glass substrate that was drawn in the molten state through a thin slot is set forth), it fails to use this substrate in the claimed method for generating an array. That is, Applicants do not even set forth one working example of an array of chemical moieties. Although the specification sets forth several potential species (e.g., biopolymers) and cite several references such as Ser. No. 09/302898 for "Polynucleotide Array Fabrication", there is no evidence that any of these chemical moieties were ever used in accordance with the claimed method.

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach this enormous genus that falls within a highly unpredictable

art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Response

5. Applicant's arguments directed to the above Enablement rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "[a]s set forth above, the Applicants disagree [that the claims encompass virtually an infinite number of substrates] and contend that the claims specifically exclude all substrates that do not possess a planar surface, those that cannot be drawn and those that are not identified as having a first direction across the substrate surface along which the substrate surface has a higher height uniformity than along a second direction" (e.g., see 3/1/07 Response, pages 12 and 13, especially page 13, first full paragraph).

[1] To the extent that Applicants' are merely repeating their previous arguments; the Examiner contends that those issues were adequately addressed above, which are

incorporated in their entireties herein by reference.

[2] Applicants argue, "the general technology of array fabrication has been around for years. In face, as evidenced by Agilent, whole industries have grown around this type of technology. For instance, academic institutions all over the nation like Stanford and Harvard regular[ly] employ these technologies in biological research. Hence, contrary to the assertion of the Office, the Applicants contend that the level of skill in the array fabrication arts is relatively high" (e.g., see 3/1/07 Response, page 13, paragraph 2).

[2] Applicants' arguments do not rise to the level of factual evidence. See MPEP § 716.01(c): The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Here, Applicants cite no references to support this conclusion (e.g., no Harvard/Stanford references). Furthermore, Applicants cite no references to refute the Examiner's references of record.

[3] Applicants argue, "[t]he specification teaches how to determine surface height variations as to generate a height uniformity ... The specification also teaches exemplary substrates which may be used in accordance with the methods of the invention ... Further still, the specification teaches how to use an inkjet printer to deposit a chemical moiety on the surface of the substrate" (e.g., see 3/1/07 Response, page 13, last paragraph).

[3] Applicant's specification sets forth only one working example of a substrate with higher height uniformity in one direction than in another (e.g., see specification, page 3, paragraph 2; see also figures 6 and 7 wherein a planar glass substrate that was drawn in the molten state through a thin slot is set forth). Although the Applicants

mention several other species that might be possible (e.g., see specification, page 21, paragraph 2 wherein both flexible and non-flexible materials are set forth including nylon, nitrocellulose, polypropylene, etc.), there is no evidence that any of these substrates were ever made and/or tested. Furthermore, there is no evidence presented that would suggest that any or all of the materials would likewise be amendable to a rolling process (like the one set forth for the drawn glass) that would impart a higher height uniformity. In addition, Applicants do not set forth any working examples of a chemical moiety. Although the specification sets forth several potential species (e.g., biopolymers such as carbohydrates, see specification, page 6, last paragraph) and cite several references such as Ser. No. 09/302898 for "Polynucleotide Array Fabrication", there is no evidence that any of these chemical moieties were ever used in accordance with the claimed method. Thus, Applicants have not even set forth a single working example of the claimed method when the chemical entities are taken into account (i.e., no quid pro quo here).

Accordingly, the Enablement rejection cited above is hereby maintained.

Claims Rejections - 35 U.S.C. 102

6. Claim 45 is rejected under 35 U.S.C. 102(b) as being anticipated by Cremer et al. (Cremer et al. "Creating spatially addressed Arrays of Planar Supported Fluid Phospholipid Membranes" *J. Am. Chem. Soc.* **1999**, *121*, 8130-8131).

For ***claim 45***, Cremer et al. (see entire document) disclose method for fabricating an array of planar supported fluid phospholipids membranes (e.g., see

Cremer et al, page 8130, column 1; see also figures 1 and 2), which anticipates the claimed invention. For example, Cramer et al. disclose **(a)** comparing height uniformity of a first direction and a second direction across a planar surface of a substrate to identify a first direction having higher height uniformity than a second direction, wherein said first and second directions are planar to said substrate (e.g., see figure 4; see also page 8131, column 2; see also figures 1-3). Here, Cremer et al. measure and compare the height of the chemical features along the surface of the planar chip in all directions. For example the height of the square wells that contain lipids is ~ 5 nm higher than the wells that do not contain a lipid bilayer (e.g., see figure 4). In addition, the hydrophobic barriers between each square well was also measured and ranged between 25 μm to 250 μm in thickness (e.g., see figure 1; see also page 8130, column 1, paragraph 2, see also page 8131, column 2, "Up to now we have experimented with square well plates from 25 μm × 25 μm to 250 μm × 250 μm with hydrophobic partitions ranging from 25 μm to 250 μm in thickness"). Thus, all heights in every direction along the planar surface were measured and compared, which would include a first and second direction. In addition, Cremer et al. disclose **(b)** placing the different chemical moieties in a row on said planar surface of the substrate lengthwise along the direction having the higher height uniformity so as to provide a row of different chemical moieties that is more closely aligned with the first direction than the second direction (e.g., see figures 2 and 3; see also page 8131, column 2). For example, three different dyes or dye mixtures were placed

in the leftmost column, which is more closely aligned in a vertical direction as opposed to a slight more skewed angle. Furthermore, this "vertical" positioning is more closely aligned with a direction that has higher height uniformity than a second "skewed" direction that does not (e.g., see 12/29/05 Office Action, page 4, figures A and B showing principle behind difference in heights along the surface of a substrate between vertically aligned, figure A, and skewed angles, figure B). In addition, Cremer et al. disclose rows that contain a plurality of spatially addressable features containing said different chemical moieties (e.g., see figures 2 and 3 showing different chemical moieties that are spatially addressable).

Response

7. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "although Cremer may have measured the dimensions o the chips and determined the depth of the hydrophobic partitions, Cremer has not determined the variations in the relative height across the surface of the substrate nor has Cremer used that determination to compare height uniformity so as to identify the direction having the higher uniformity so as to place chemical moieties on the surface in a row along the direction having the higher uniformity. Specifically, there is no teaching within

Cremer with regard to the variation of substrate surface height or placing chemical moieties on the surface of a substrate based on a comparison of uniformity height." (e.g., see 3/1/07 Response, pages 14-16, especially page 15, last full paragraph).

[1] The Examiner respectfully disagrees. For example, Cramer et al. disclose **(a)** comparing height uniformity of a first direction and a second direction across a planar surface of a substrate to identify a first direction having higher height uniformity than a second direction, wherein said first and second directions are planar to said substrate (e.g., see figure 4; see also page 8131, column 2; see also figures 1-3). Here, Cremer et al. measure and compare the height of the chemical features along the surface of the planar chip in all directions. For example the height of the square wells that contain lipids is ~ 5 nm higher than the wells that do not contain a lipid bilayer (e.g., see figure 4). In addition, the hydrophobic barriers between each square well was also measured and ranged between 25 μm to 250 μm in thickness (e.g., see figure 1; see also page 8130, column 1, paragraph 2, see also page 8131, column 2, "Up to now we have experimented with square well plates from 25 μm × 25 μm to 250 μm × 250 μm with hydrophobic partitions ranging from 25 μm to 250 μm in thickness"). Thus, all heights in every direction along the planar surface were measured and compared, which would include a first and second direction. In addition, Cramer et al. use this knowledge as a "basis" for **(b)** placing the different chemical moieties in a row on said planar surface of the substrate lengthwise along the direction having the higher height uniformity so as to provide a row of different chemical moieties that is more closely aligned with the first direction than the second direction (e.g., see figures 2 and 3; see also page 8131, column 2).

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained.

Claim Rejections - 35 USC § 103

8. Claims 28 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cremer et al. (Cremer et al. "Creating spatially addressed Arrays of Planar Supported Fluid Phospholipid Membranes" *J. Am. Chem. Soc.* **1999**, *121*, 8130-8131) in view of Lemmo et al. (Lemmo et al. Anal. Chem. **1997**, *69*, 543-551) and Baldeschwieler et al. (WO 95/25116) (Date of Patent is **September 21, 1995**) (2/21/02 IDS, entry 1L).

For ***claim 45***, Cremer et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claim 45. Connell v. Sears, Roebuck & Co., 722 F.2d 1542, 1548 (Fed. Cir. 1983) ("anticipation is the epitome of obviousness"); see also see In re Skoner, 517 F.2d 947, 950, 186 USPQ 80, 83 (CCPA 1975); In re Pearson, 494 F.2d 1399, 1402, 181 USPQ 641, 644 (CCPA 1974).

The prior art teachings of Cremer et al. differ from the claimed invention as follows:

For ***claim 28***, Cremer et al. are fails to teach the use of a pulse-jet printer to deposit the different chemical moieties.

However, the combined references of Lemmo et al. and Baldeschwieler et al. teach the following limitations that are deficient in Cremer et al.:

For ***claim 28***, the combined references of Lemmo et al. and Baldeschwieler et al. (see entire documents) teach the use of a pulse-jet printer for the synthesis of combinatorial libraries (e.g., see Lemmo et al., abstract; see also figure 2; see also page

544, column 1, paragraph 2 wherein piezoelectric devices are disclosed; see also Baldeschwieler et al., figure 2; see also page 16, line 25; see also Example 1; see also Applicants' specification, page 13, paragraph 3, which defines pulsejet printers to include piezoelectric devices commonly found in inkjet printers).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a pulse jet printer as taught by the combined references of Lemmo et al. and Baldeschwieler et al. to make the spatially addressable arrays as taught by Cremer et al. because Cremer et al. state that pulsejet printers can be used for this purpose and explicitly cite the Lemmo et al. in support of this position (e.g., see Cremer et al., page 8131, column 2, "Incorporating new deposition technologies such as the chemical inkjet microdispenser should allow very large membrane libraries to be created on experimentally practical time scales"). Furthermore, a person of ordinary skill in the art would have been motivated to use a pulsejet printer to create large libraries on an "experimentally practical time scale" (e.g., see Cremer et al., page 8131, column 2). In addition, Cremer et al. state, "the microdispenser could [also] serve as a convenient method for depositing premixed concentration arrays of three or four component membranes" (e.g., see Cremer et al., page 8131, column 2). Moreover, the pulse jet printer represents a "non contact" method of deposition that will not harm the substrate or contaminate adjacent wells. Finally, a person of ordinary skill in the art would reasonably have expected to be successful because inkjet printers were routinely used for making material libraries.

Response

9. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "[a]s set forth above, an element of the rejected claims is comparing height uniformity ... As described above, Cremer is deficient ... Lemmo and Baldeschwieler were cited solely for their disclosure of the use of a pulse jet printer [and, as a result] the fail to remedy the deficiencies of Cremer" (e.g., see 3/1/07 Response, pages 16 and 17, especially page 16, last paragraph).

[1] To the extent that Applicants are merely repeating their previous arguments under 35 U.S.C. § 102, the Examiner contends that those arguments were adequately addressed above, which are incorporated in their entireties herein by reference. Thus, Cremer is not deficient and Applicants' arguments with regard to Lemmo and Baldeschwieler are moot.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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April 9, 2007

JON EPPERSON
PRIMARY EXAMINER